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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,980	10/26/2005	Martin Alan Lee	41577/314737	9249

23370 7590 07/25/2008

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EXAMINER	
BAUGHMAN, MOLLY E	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
07/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,980	LEE ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-83,85 and 86* is/are pending in the application.

4a) Of the above claim(s) *72-83* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-71 and 85-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments to claims 43-71, cancellation of claim 84, and addition of claims 85-86 in the reply filed on 4/3/08 are acknowledged.

Response to Arguments

2. Applicant's arguments, see pg.12, filed 2/28/08, with respect to objections to the specification, specifically, to the title, have been fully considered and are persuasive in view of the amendments made to the title. The objection of the specification has been withdrawn.

3. Applicant's arguments, see pg.12, filed 2/28/08, with respect to rejection of claim 44 under 35 USC § 112, second paragraph, have been fully considered and are persuasive. The rejection of claim 44 has been withdrawn. However, upon further consideration, new grounds of rejection have been made over new claim 86.

4. Applicant's arguments, see pg.12-18, filed 2/28/08, with respect to the following rejections:

a. Claim 84 is rejected under 35 U.S.C. 102(b) as being anticipated by Fisher et al. (US 5,491,063).

b. Claims 43-44, 48-69 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 99/28500) in view of Marrazza et al., "Disposable DNA electrochemical sensor for hybridization detection," Biosensors and Bioelectronics, 1999, Vol.14, pp.43-51.

c. Claims 43-46, and 48-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 99/28500) in view of Yun et al. (US 7,090,977 B2, priority date 10/30/01).

d. Claims 45-47, and 70-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 99/28500) in view of Marrazza et al. (1999), as applied to claims 43-44, 48-69 and 84 above, and further in view of Patterson (US 5,132,327).

e. Claims 47, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 99/28500) in view of Yun et al. (US 7,090,977 B2, priority date 10/30/01), as applied to claims 43-46, 48-70 above, and further in view of Patterson (US 5,132,327).

have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Lee et al. (WO/99/28500, of record) and Smith et al., "Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-drug resistant small cell lung cancer cells," Biochem. Pharma. 1990, Vol.40, No.9, pp.2069-2078.

5. Applicant's arguments, see pg.13, filed 2/28/08, with respect to the rejection(s) of claim(s) 43-44, 48-55, and 57-69 under 35 USC § 102(e), Lee (US 2004/0241679, priority date 5/25/01) have been fully considered, but are not persuasive. Applicants argued that the new amendment to claim 43, the addition of "are not detectable in the

context of the method" in relation to the DNA duplex binding agent emissions, overcomes Lee et al. because Lee requires fluorescence energy emissions from both the donor and acceptor during the method since it is based on a FRET assay. This is not found persuasive because although there is fluorescence energy transfer from the donor (in some embodiments various fluorophores) to the acceptor (ethidium bromide in one embodiment), the method is based on the ability of an acceptor (ethidium bromide) to quench the fluorescence from a donor (various fluorophores), where the method measures such quenching by measuring the fluorescence of the donor over time. With that said, Lee states that it is also possible to only measure emission from one label (either the donor or acceptor) in cases where the donor and acceptor labels have little or no overlap in emission wavelengths. Although Lee exemplifies measuring fluorescence from the acceptor only in this regard (see paragraph [0045]), one of skill would reason that measurement from the donor only was also included under this embodiment. Since various fluorophores and ethidium bromide have different emission wavelengths, the method of Lee et al. includes measuring emissions from only the donor (i.e. fluorophores), whereby the emission of the acceptor *is not detectable in the context of the method.*

6. Applicant's arguments, see pg.18-19, filed 2/28/8, with respect to the rejection(s) of claim(s) 43-44 and 48-69 under nonstatutory obvious-type double patenting over claims 1-4, 6-7, 9, and 10-14 of copending application 10/478,788 have been fully considered, but they are not persuasive. Applicants argued that the claims have been

amended to state that the emissions of the DNA duplex binding agent are not detectable within the context of the method. This is not found persuasive because as explained in the genus-species relationship, claim 9 of the '788 application states that such DNA duplex binding agents can be those which are dark acceptors, which by definition does not have emissions which are detectable within the context of the method, being that they are *dark acceptors*.

7. Applicant's arguments, see pg. 19, filed 2/28/8, with respect to the rejection(s) of claim(s) 43-46 and 48709 under nonstatutory obvious-type double patenting over claims 1-2, 4-9, and 11-13 of US 6,833,257 (Lee II) in view of Yun, have been fully considered and are persuasive. Therefore the rejection has been withdrawn. However, upon further consideration, new grounds of rejection have been made in view of Smith et al., "Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-drug resistant small cell lung cancer cells," Biochem. Pharma. 1990, Vol.40, No.9, pp.2069-2078.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 86 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

regards as the invention. Claim 86 is drawn to the method of claim 66 where in the DNA duplex binding agent does not emit visible light, however, claim 66 requires that the DNA duplex binding agent does not emit radiation in the visible range of the spectrum. It is unclear how these two differ, as "visible light," by definition is radiation or wavelengths in the visible range of the spectrum. Clarification is required.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 43-44 and 48-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (WO/99/28500, of record).

Regarding claim 43, Lee et al. teach a method for detecting the presence of a target nucleic acid sequence in a sample, said method comprising: (a) adding to a sample suspected of containing said target nucleic acid sequence, a fluorescently labelled probe specific for said target sequence, and a DNA duplex binding agent which can absorb fluorescent energy from the fluorescent label on the probe, wherein emission from the DNA duplex binding agent are not detectable in the context of the method (b) subjecting the thus formed mixture to all amplification reaction in which target nucleic acid is amplified, (c) subjecting said sample to conditions under which the said probe hybridises to the target sequence, and (d) monitoring fluorescence from said

sample (see abstract; pg.6, lines 4-17; pg.7, lines 1-3; pg.14, lines 20-32, specifically, see pg.11 where Lee discusses the embodiment where the donor and acceptor do not have overlapping wavelengths and measurement can take place by measuring the emissions from one of the labels at a particular wavelength. Although Lee discusses fluorescein and ethidium bromide, where measurement is taken from EtBr as 1/fluorescein, one of skill could reason that the embodiment also included measuring only emission from fluorescein. In this case, the emissions from EtBr are not detectable in the context of the method).

Regarding claim 44, Lee teaches DNA duplex binding agents having a fused conjugated ring system (i.e. EtBr).

Regarding claim 48, Lee teaches the method according to claim 43 wherein the target nucleic acid is rendered single stranded prior to hybridization to the probe in step (c) (pg.8, lines 4-8).

Regarding claim 49, Lee teaches the method wherein the amplification reaction is the polymerase chain reaction (PCR) (pg.8, lines 21-23).

Regarding claim 50 and 51, Lee teaches the method wherein the probe hybridizes with the target nucleic acid during every cycle of the amplification reaction and wherein the fluorescence from the sample is monitored throughout the amplification reaction (pg.8, lines 30-38; pg.9, lines 1-14).

Regarding claim 52 and 53, Lee teaches the method wherein fluorescence data generated is used to determine the rates of probe hybridization and where the

fluorescence data is used to quantitate the amount of target nucleic acid present in the sample (pg.9, lines 25-38; pg.10, lines 1-17).

Regarding claims 54-55, Lee teaches the method wherein the fluorescent label is a rhodamine dye, Cy5, fluorescein or a fluorescein derivative and wherein the fluorescent label is attached at an end region of the probe (pg.10, lines 28-37).

Regarding claim 56, Lee teaches the method wherein the fluorescent label is attached at the 3'end of the probe and prevents extension thereof by a polymerase (pg.12, lines 30-34).

Regarding claim 57, Lee teaches the method wherein the probe is designed such that it is released intact from the target sequence during a phase of the amplification process other than the extension phase (pg.12, lines 20-24).

Regarding claim 58, Lee teaches the method wherein the probe is released intact from the target sequence during the extension phase of the amplification process by the action of the polymerase, and the amplification reaction is effected using a polymerase which lacks 5'-3' exonuclease activity (pg.12, lines 15-18, 25-29).

Regarding claim 59, Lee teaches a method according to claim 43 which comprises performing nucleic acid amplification on a target polynucleotide in the presence of (a) a nucleic acid polymerase (b) at least one primer capable of hybridizing to said target polynucleotide, (c) an oligonucleotide probe which is capable of binding to said target polynucleotide sequence and which contains a fluorescent label and (d) a DNA duplex binding agent which is capable of absorbing fluorescent energy from the said fluorescent label, and which does not emit light in the visible range of the spectrum;

and monitoring changes in fluorescence during the amplification reaction (see abstract; pg.6, lines 4-17; pg.7, lines 1-3; pg.14, lines 20-32, specifically, see pg.11 where Lee discusses the embodiment where the donor and acceptor do not have overlapping wavelengths and measurement can take place by measuring the emissions from one of the labels at a particular wavelength. Although Lee discusses fluorescein and ethidium bromide, where measurement is taken from EtBr as 1/fluorescein, one of skill could reason that the embodiment also included measuring only emission from fluorescein. In this case, the emissions from EtBr are not detectable in the context of the method).

Regarding claim 60, Lee teaches the method wherein the amplification is suitably carried out using a pair of amplification primers (pg.13, lines 34-35).

Regarding claim 61, Lee teaches the method wherein the nucleic acid polymerase is a thermostable polymerase (pg.14, lines 1-2).

Regarding claims 62-65, Lee teaches the method wherein in a further step, a hybridisation assay is carried out and a hybridization condition which is characteristic of the sequence is measured [i.e. claim 62], wherein the condition is temperature, electrochemical potential, or reaction with an enzyme or chemical [i.e. claim 63-64], and wherein the method is used to detect allelic variation or a polymorphism in a target sequence [i.e. claim 65] (pg.14, lines 34-37; pg.15, lines 1-31).

Regarding claim 66, Lee teaches a method comprising a) adding to a sample suspected of containing said sequence, a fluorescently labelled probe specific for said target sequence and a DNA duplex binding agent able to absorb fluorescence from a fluorescent label on the probe but which does not emit radiation in the visible range of

the spectrum, (b) subjecting said sample to conditions under which the said probe hybridizes to the target sequence, (c) monitoring fluorescence from said sample and determining a particular reaction condition, characteristic of said sequence, at which fluorescence changes as a result of the hybridization of the probe to the sample or destabilization of the duplex formed between the probe and the target nucleic acid sequence (see abstract; pg.6, lines 4-17; pg.7, lines 1-3; pg.14, lines 20-32; pg.14, lines 34-37; pg.15, lines 1-31; pg.17, lines 4-21).

Regarding claims 67-69, Lee teaches a method wherein the reaction condition characteristic of said sequence is temperature, electrochemical potential, or reaction with an enzyme or chemical, and wherein the results obtained from two sequences are compared in order to determine the presence of polymorphisms or variations therebetween (pg.14, lines 34-37; pg.15, lines 1-31).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 45-47, 66-71, and 85-86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO/99/28500, of record) in view of Smith et al., "Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-drug resistant small cell lung cancer cells," Biochem. Pharma. 1990, Vol.40, No.9, pp.2069-2078.

The teachings of the primary reference are discussed above. This reference does not teach the method where the DNA duplex binding reagent does not emit radiation in the visible range of the spectrum [claim 66, 85-86], is mitoxantrone or its salt, or nogalamycin or daunomycin [claim 45-46, 70]; or is a compound having the formula according to claim 47 [claim 47, 71].

. Smith et al. teach mitoxantrone, which is a DNA intercalator (i.e. DNA duplex binding agent). Smith et al. demonstrate through a flow cytometric assay that mitoxantrone is able to quench fluorescence from Ho33342 dye labeled cells (see Figure 7a and b; pg.2071, "Flow cyotmetric analysis of mitoxantron-DNA interaction by Ho33342-DNA," and pg.2075, left column). Mitoxantrone inherently does not emit light within the visible range of the spectrum, has a fused conjugated ring system, and has the formula according to claim 47.

One of ordinary skill in the art would have been motivated to modify the method of Lee et al. to use a DNA duplex binding agent which does not emit visible light (or radiation in the visible range of the spectrum) because Smith demonstrates the use of mitoxantrone as a DNA intercalator and a fluorescence quencher which does not emit visible light. Since Lee demonstrates the benefits of using DNA duplex binding agents (as acceptors) that do not have emissions or wavelengths that overlap to that of donors during a FRET assay, such that one only has to measure the emission of the donor label for detection and there is little or no background, and Smith demonstrates that it was conventional in the art at the time of the invention to use mitoxantrone as a DNA duplex binding agent and fluorescence quencher, it would have been obvious to one skilled in the art to substitute one DNA duplex binding agent for the other to achieve the predictable result of being able to measure emissions from only one label (i.e. the donor) and reduce background during the assay.

15. Claims 45-47, 66-71, and 85-86 are rejected under 35 U.S.C. 103(a) as being obvious over Lee (US 2004/0241679, priority date 5/25/01), in view of Smith et al., "Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-drug resistant small cell lung cancer cells," Biochem. Pharma. 1990, Vol.40, No.9, pp.2069-2078.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome

by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of the primary reference are discussed above. This reference does not teach the method where the DNA duplex binding reagent does not emit radiation in the visible range of the spectrum [claim 66, 85-86], is mitoxantrone or its salt, or nogalamycin or daunomycin [claim 45-46, 70]; or is a compound having the formula according to claim 47 [claim 47, 71].

. Smith et al. teach mitoxantrone, which is a DNA intercalator (i.e. DNA duplex binding agent). Smith et al. demonstrate through a flow cytometric assay that mitoxantrone is able to quench fluorescence from Ho33342 dye labeled cells (see Figure 7a and b; pg.2071, "Flow cyotmetric analysis of mitoxantron-DNA interaction by Ho33342-DNA," and pg.2075, left column). Mitoxantrone inherently does not emit light

within the visible range of the spectrum, has a fused conjugated ring system, and has the formula according to claim 47.

One of ordinary skill in the art would have been motivated to modify the method of Lee et al. to use a DNA duplex binding agent which does not emit visible light (or radiation in the visible range of the spectrum) because Smith demonstrates the use of mitoxantrone as a DNA intercalator and a fluorescence quencher which does not emit visible light. Since Lee demonstrates the benefits of using DNA duplex binding agents (as acceptors) that do not have emissions or wavelengths that overlap to that of donors during a FRET assay, such that one only has to measure the emission of the donor label for detection and there is little or no background, and Smith demonstrates that it was conventional in the art at the time of the invention to use mitoxantrone as a DNA duplex binding agent and fluorescence quencher, it would have been obvious to one skilled in the art to substitute one DNA duplex binding agent for the other to achieve the predictable result of being able to measure emissions from only one label (i.e. the donor) and reduce background during the assay.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 43-46, and 48-70 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-9, 11-13 are of U.S. Patent No. 6,833,257 in view of Smith et al., "Mitoxantrone-DNA binding and the induction of Topoisomerase II associated DNA Damage in Multi-drug resistant small cell lung cancer cells," Biochem. Pharma. 1990, Vol.40, No.9, pp.2069-2078. Although the conflicting claims are not identical, they are not patentably distinct from each other because of a genus: species relationship. For instance, Claim 1 of the '257 patent recites:

"A method for detecting the presence of a target nucleic acid sequence in a sample, said method comprising: (a) adding to a sample suspected of containing said nucleic acid sequence, a DNA duplex binding agent, and a probe specific for said target sequence, said probe comprising a reactive molecule able to absorb fluorescence from or donate fluorescent energy to said DNA duplex binding agent, wherein the 3' end of the probe is blocked to inhibit extension thereof during the extension phase, (b)

subjecting the thus formed mixture to an amplification reaction in which the target nucleic acid is amplified, (c) subjecting said sample to conditions under which the said probe hybridizes to the target sequence, and subsequently releasing said probe intact from the target sequence, and (d) monitoring fluorescence from said sample associated with one or both of the hybridization of the probe to the target sequence and the dissociation of the probe from the target sequence."

While the claim of the '257 patent is drawn to a method where the energy is donated to the DNA duplex binding agent, and the specification is drawn to DNA duplex binding agents which have a fused conjugated ring system (i.e. ethidium bromide), it does not specifically discuss those which do not emit visible light.

Smith et al. teach mitoxantrone, which is a DNA intercalator (i.e. DNA duplex binding agent). Smith et al. demonstrate through a flow cytometric assay that mitoxantrone is able to quench fluorescence from Ho33342 dye labeled cells (see Figure 7a and b; pg.2071, "Flow cyotmetric analysis of mitoxantron-DNA interaction by Ho33342-DNA," and pg.2075, left column). Mitoxantrone inherently does not emit light within the visible range of the spectrum, has a fused conjugated ring system, and has the formula according to claim 47.

Summary

18. No claims are free of the prior art.

19. Any remaining rejections and/or objections not addressed above are withdrawn in view of the amendments and/or arguments.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is (571)272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637

/Molly E Baughman/
Examiner, Art Unit 1637